PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/052104	09.09.2004	10.09.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/16, C08J3/12

Applicant
JANSSEN PHARMACEUTICA N.V.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Epskamp, S

Telephone No. +31 70 340-2857

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/052104

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,3,5,6,9
	No:	Claims	1,4,7,8
Inventive step (IS)	Yes:	Claims	9
	No:	Claims	1-8
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document/s/:

D1: BASF ExAct No. 5 (2000), p. 6-7: Kollidon® VA 64: An excellent dry binder. Retrieved from the Internet on 29/9/2005, http://www.pharma-solutions.basf.com/(mck0o54541nxg555xxqywy45)/pdf/ExAct/kollidon_va_64/09007ac78000e871.pdf

D2: US 6,318,650 B

Clarity

1 - The term "platelets" as used in claims 1 and 4 is vague and unclear, and does not allow the reader to define the scope of protection sought (Art 6 PCT). The definition on page 12, lines 12-14, makes clear that according to the applicant any particle with a thickness smaller than its length and width is considered a platelet. It would appear that any particle which is not a perfect sphere or cube would fall under such a definition.

2 - Claims 1-4 further lack clarity, as the polymers referred to therein are not adequately defined (Art 6 PCT).

In claims 1, 2 and 4, a polymer PVP-VA-60 is referred to. However, no such polymer appears to exist (compare the description, page 11, lines 5-6). Given the description it was assumed that PVP-VA 64 was meant.

In claims 1, 3 and 4, Eudragit-E100-PO is referred to. The use of a trademark in the claims leads to a lack of clarity, as it may not be guaranteed that the product referred to is not modified while maintaining its name during the term of the patent. Furthermore, documentation of the manufacturer only appears to refer to either Eudragit E100 (available as granules), or Eudragit E PO (powder), not to Eudragit-E100-PO. In any case, using the tradename as is done in the claims could also be seen as contradicting the fact that the particles should be shaped as platelets, since the tradename already implies a physical form (granules or powder).

Novelty

3 - Furthermore, the above-mentioned lack of clarity notwithstanding, the subject-matter of claims 1, 4, 7 and 8 is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.

4 - Document D1 (page 6, middle column, par. 4; figure 2) shows that particles of Kollidon

VA 64 (PVP VA 64) have a "shell like structure". Indeed, the shape of at least some of the particles shown in figure 2 is such, that the term "platelets" is not sufficiently well-defined to distinguish the particles of claim 1 from these particles (see point 1 above).
Consequently, claim 1 lacks novelty over D1.

5 - Document D2 (column 1, lines 43-59; examples; figure 1; claims) discloses a process for producing solid particulate preparations in which a bioactive substance is homogeneously dispersed in a matrix of thermoplastic excipients. The particles are prepared in a screw extruder by melting the excipients and mixing them with the active substance, followed by cooling the mixture and grinding it to a powder in a cooling zone of the extruder. In examples 4, 7 and 9, Kollidon VA 64 is used as excipient, the use of acrylic polymers is also foreseen (column 6, lines 57-58; example 8). Given the process, at least some of the particles will have a shape which would fall under the definition for platelets given in the application (see point 1 above).
Thus, claims 4, 7 and 8 are considered to lack novelty over D2.

6 - Claims 2, 3, 5, 6 and 9, as far as clear, are considered novel.

Inventive Step

7 - Lacking novelty, claims 1, 4, 7 and 8 cannot be considered inventive (Art 33(3) PCT).

8 - Document D2 (see point 5 above) is the closest state of the art for the subject-matter of claim 9.
Claim 9 differs from D2, in that a pressurized gas is injected into the barrel of the melt extruder, followed by mixing and expanding the mixture of PVP-VA 60 or Eudragit E100 PO, (active ingredient) and gas. Furthermore a melt seal is created before the site of the gas injection.
The problem to be solved by claim 9 in view of D2 is to provide a process for forming particles, the particles having improved compressibility and being easier to mill.
Claim 9 is considered inventive (Art 33(3) PCT). Document D2 already foresees adding a (gaseous) blowing agent to the molten polymer/drug mixture, which leads to foam formation in the cooling zone of the extruder, and to more efficient comminution there (column 3, lines 23-37; column 8, line 31). However, following this suggestion of D2 indeed leads to the more comminuted particles, not necessarily to the particles resulting from the process of claim 9 which are easier to mill (in other words: which still can be milled further) and have a better compressibility. So the skilled person would not apply the suggestion to add a (gaseous) blowing agent to a molten mixture of PVP-VA 64 or acrylic polymer and

drug, to make particles which have a better compressibility and are easier to mill, as compared to the process without the addition of gas.

9 - Dependent claims 2, 3, 5 and 6 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step with respect to the prior art named in the present proceedings. The reasons therefor are that the additional features of the said dependent claims are either directly known from document D2, or are a combination of features obvious to the skilled person in consideration of documents D1-D2, or they concern minor modifications which lie within the normal practice of the skilled person and/or for which nu (unexpected) technical effect has been shown.

Industrial applicability

10 - Claims 1-9 fulfill the requirements of Article 33(4) PCT.